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CASE REPORT

Exacerbation of Fibrous Dysplasia Associated With an Adolescent Pregnancy

CATHERINE STEVENS-SIMON, M.D., JANET STEWART, M.D.,
IDA I. NAKASHIMA, M.D., AND MARGUERITTE WHITE, M.D.

Fibrous dysplasia is a metabolic skeletal disorder in which the medullary spaces of affected bones are replaced by fibro-osseous tissue. Patients with fibrous dysplasia usually become symptomatic during childhood; the adolescent patient we describe is unusual because she was not known to suffer from fibrous dysplasia until she became pregnant and experienced a dramatic reactivation of the symptoms. The therapeutic implication of this case and reproductive counselling for young women with fibrous dysplasia are discussed.

KEY WORDS:
Fibrous dysplasia
Adolescent pregnancy
Contraception

Fibrous dysplasia is a metabolic skeletal disorder in which the medullary spaces of affected bones are replaced by fibro-osseous tissue (1,2). The bony abnormality can affect one (monostotic fibrous dysplasia) or many bones (polyostotic fibrous dysplasia), and may be associated with irregular cutaneous pigmentations (café-au-lait spots) and endocrine abnormalities (the McCune-Albright syndrome). Patients with fibrous dysplasia usually become symptomatic during childhood; the adolescent patient we describe is unusual because she was not known to suffer from fibrous dysplasia until she became pregnant and experienced a dramatic reactivation of the symptoms.

From The Departments of Pediatrics (C.S.S., J.S., I.N.) and Obstetrics and Gynecology (M.W.), University of Colorado Health Science Center, Denver, Colorado.

Address reprint requests to: Catherine Stevens-Simon, M.D., The Children's Hospital, 1056 East 19th Avenue, Denver, CO 80218.

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Case Report

A 17-year-old, nulliparous, white female came to the Colorado Adolescent Maternity Program in her 30th week of pregnancy; she complained of approximately 2 weeks of progressive, painless swelling in the right frontal and right and left parietal regions of her skull. There was no history of trauma. The patient reported that at 4 years of age a similar bony swelling had appeared in the occipital region of her skull. Studies performed at that time were said to have been nondiagnostic; no further studies were performed during the ensuing 13 years because there was no progression of the bony abnormality.

The patient described normal pubertal development; menarche occurred at 12.5 years of age. She denied abnormal skin pigmentations, related no history of gastrointestinal problems, renal disorders, pathologic fractures, or bone pain but stated that she had a "nodule" removed from her thyroid gland at 2 years of age. In addition she complained of increasing impairment of vision and hearing in her right eye and ear, respectively, but had not had these symptoms evaluated by a medical professional. She took no medications except prenatal vitamins. There was no family history of bone disorders or precocious puberty.

The results of the physical examination were unremarkable for a woman in the third trimester of pregnancy, except that her skull was deformed by four focal, smooth, nontender bony protuberances. These were located in the occipital, right frontal, and right and left parietal regions of her skull. A roent-

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genograph revealed marked bony thickening and multiple radiolucent lesions in a pattern characteristic of fibrous dysplasia (2).

The patient did well during pregnancy, the bony abnormalities did not progress and labor began spontaneously at term, resulting in the birth of a normal 3289 g male infant.

Following delivery a complete skeletal survey was obtained. The study revealed no additional areas of fibrous dysplasia or other bony abnormalities. The alkaline phosphatase level which was also obtained at this time was slightly above normal: 130 (normal being less than 118). The patient was fitted for a diaphragm and continued to do well until her second postpartum month when she began to complain of increasingly frequent and severe headaches, and localized pain over the occipital lesion. She described no new visual or auditory symptoms, and her physical examination remained unremarkable.

To evaluate these symptoms a magnetic resonance (MRI) imaging study of the cranium was obtained and the patient was examined by a neurosurgeon, an ophthalmologist, and an otolaryngologist. The MRI study (Figure 1) revealed that the middle table of the skull was extensively involved with an expansile bone-centered process. These changes were most notable in the greater wing of the sphenoid, the right temporal, frontal, and the occipital bones; and were associated with upward displacement of the pituitary gland and a mild inward deformity of the adjacent right frontal cerebral surface. The optic and otic nerves were not directly involved. As there was no cranial nerve entrapment, surgery was not recommended and a conservative management approach was adopted. The patient's symptoms gradually improved and she has been followed expectantly for exacerbations which might possibly necessitate surgical intervention.

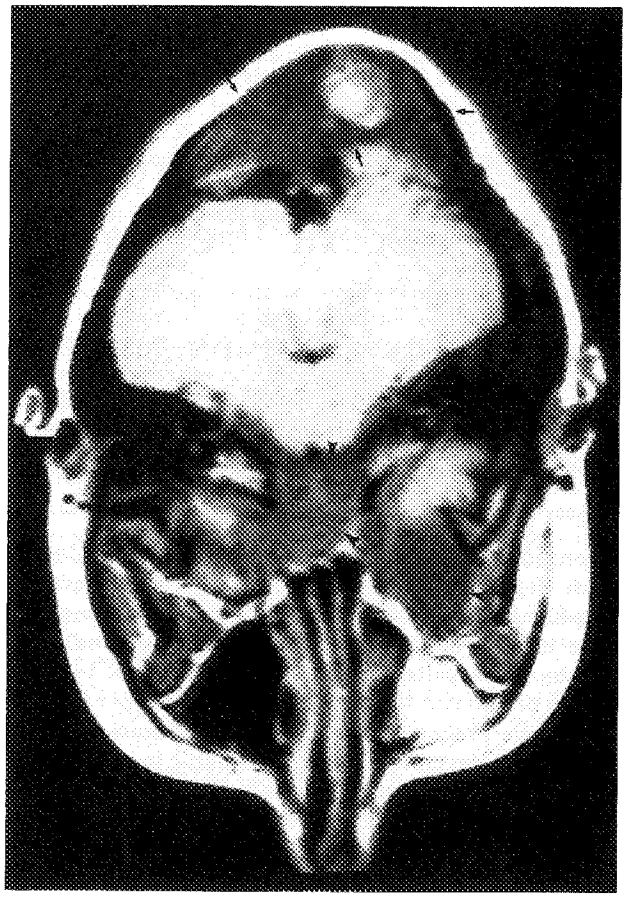

Figure 1. *Axial T_1-weighted magnetic resonance image of the head. Sections at the level of the cerebellum demonstrate an expansile mixed-intensity lesion centered in the middle table of the occiput (arrows). There is extensive additional involvement of the skull base (arrow heads).*

Discussion

Fibrous dysplasia is a relatively common nonfamilial bone disease which usually becomes symptomatic in late childhood: on average at 10 years of age (1). In most cases the condition affects only one bone (monostotic fibrous dysplasia) but multiple bones can be affected (polyostotic fibrous dysplasia). Irregular areas of skin pigmentation (café-au-lait spots) and elevated serum alkaline phosphatase levels are coexistent findings in approximately one third of patients with the polyostotic form of fibrous dysplasia; the complete McCune-Albright syndrome (polyostotic fibrous dysplasia, café-au-lait spots, and precocious pseudopuberty) is found in only a minority of affected individuals.

In fibrous dysplasia the marrow is replaced by a highly vascular fibrous tissue in which small islands of cartilage and bone spicules are imbedded. This benign metabolic bone disorder produces localized areas of bone growth and enlargement; affected bones are eroded and expanded from within so the normal bone cortex becomes elevated and thinned. Roentgenographic studies of bones affected by fibrous dysplasia reveal radiolucent, cystic medullary spaces, sharply demarcated by thickened, sclerotic cortical bone; the appearance is often sufficiently characteristic to establish the diagnosis (2).

Although gonadal steroids profoundly affect bone metabolism (3,4) exacerbation of fibrous dysplasia during pregnancy appears to be a rare phenomenon (1,3,5). Reactivation and progression of fibrous dysplasia in association with oral contracep-

tive therapy (6) and during puberty also appears to be rare (1,3,4). Unusually high concentrations of estrogen receptors have been found on osteogenic cells obtained from abnormal areas of the skeleton of a patient with the McCune-Albright syndrome (3) and patients with monostotic fibrous dysplasia (4). This suggests a direct etiologic connection between the hormonal fluctuations associated with pregnancy, oral contraceptive use, and puberty and the bony manifestations of the McCune-Albright syndrome (3) and of monostotic fibrous dysplasia (4). Our patient's clinical presentation is consistent with the results of these biochemical studies (3,4). High concentrations of estrogen receptor appear to be limited to osteogenic cells obtained from involved areas of the skeletons of patients with fibrous dysplasia. This case is particularly interesting because our patient did not have the McCune-Albright syndrome, had no progression of fibrous dysplasia during puberty, and was unaware that she had fibrous dysplasia until she experienced a dramatic exacerbation during pregnancy. Her clinical presentation emphasizes the importance of reproductive counseling for young women with fibrous dysplasia.

There is no evidence that prevention of pregnancy prevents progression of fibrous dysplasia and only a few case reports link exacerbations of fibrous dysplasia to pregnancy (3,5) or the use of hormonal contraceptives (6). Nevertheless, available biochemical data (3,4) suggest that it would be prudent for physicians caring for young patients with fibrous dysplasia to define the extent of skeletal involvement radiographically and to advise young women with potentially disfiguring lesions that exacerbation may occur during pregnancy (3,5) and/or in association with the use of hormonal contraceptives (6). The paucity of clinical data relating exacerbations of fibrous dysplasia to pregnancy and other circumstances in which patients are exposed to unusually high levels of gonadal steroids and our patient's own asymptomatic puberty suggest that the presence of estrogen receptors on osteogenic cells affected by fibrous dysplasia is variable. Further research is needed to define which patients with fibrous dysplasia are at risk for exacerbation during pregnancy and/or in association with the use of hormonal contraceptives. Bone biopsy followed by tests for estrogen receptors may help define individual risks and management plans.

The bony exostoses of fibrous dysplasia are usually painless but may cause local pain and tenderness; patients with cranial and facial involvement often complain of headaches, neuralgias, and visual symptoms (1,2). The etiology of the pain described by patients with cranial fibrous dysplasia remains obscure; however the results of the MRI study we performed on our patient suggest that rapid bone growth and inward bony expansion compress the dura and the adjacent brain surface, causing periosteal stretching and possibly the headaches and localized pain our patient described. Case reports of acute optic nerve compression and loss of vision make close ophthalmologic follow up a necessity for patients like ours.

Malignant degeneration is reported to occur in approximately 1 of 200 patients with fibrous dysplasia; those at highest risk are males, patients with craniofacial involvement, and patients with rapid, painful bone growth and elevated alkaline phosphatase levels. Osteogenic sarcoma is the most common malignancy, followed by fibrosarcomas (1). Our patient's presentation was particularly concerning because she described many of these symptoms and she experienced rapid, painful growth of cranial lesions. Excisional biopsy therefore remains a therapeutic option for her.

Spontaneous involution or regression of fibrous dysplasia has not been reported. The results of nonsurgical treatments are disappointing; radiotherapy is ineffective and may increase the risk of malignancy and other medical therapies may temporarily relieve pain but do not alter the progression of the disease. The surgical treatment of fibrous dysplasia has been reviewed in detail. Specific indications for surgical intervention include correction of disfiguring deformities and pathologic fractures, relief of pain, and decompression of entrapped nerves to prevent visual or hearing loss (1).

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